REMARKS

Applicant intends this response to be a complete response to the Examiner's **29 September 2010** Non-Final Office Action. Applicant has labeled the paragraphs in his response to correspond to the paragraph labeling in the Office Action for the convenience of the Examiner.

DETAILED ACTION

Preliminary Statement

Applicants have noted a claim numbering problem and note that there are two claims number 42 and not claims 45. Applicants have renumbered the claims so that the second claim number 42 is not 43 and 43 is 44 and 44 is 45. The remainder of the claims are properly numbered. Applicants' attorney apologizes for any inconvenience caused by the missing numbering.

The Examiner states as follows:

> This action is in response to communications filed 07 April 2010 accompanied by a petition to revive the application. Previously raised rejection of claims 1 and 17 under the first paragraph of35 U.S.C. 112 for new matter have been withdrawn in view ofthe amendments. However, new grounds of rejection under the first paragraph of35 U.S.C. 112 are presented as applicable to claims 1 and 35-53.

Applicants acknowledge these statements.

Response to Arguments

The Examiner states as follows:

> Applicant's remarks have been fully considered but they are not persuasive and/or are moot in view of new grounds of rejection.
>
> Regarding applicant's remarks directed to monitoring changes in risk over time with different scans performed at each time, while such features have been introduced into the claim(s), this methodes) disclosed in applicant's specification are not particular to this feature. This feature warrants new grounds of rejection.
>
> Regarding the contention that cardiovascular risk is only assessed based on calcium density in Hu, it is pointed out that Hu constructs image(s) of the region(s) of interest that indicate the attenuation profile of the region of interest and aid in identifying calcification (or scorable regions of interest or spots within the image) within the image to assess density, as in col. 1, lines 60-63 and col. 3, lines 48-53. A total calcium score is determined by summing the scores of the individual regions of interest, which indicates a risk as claimed. A density score is determined for each pixel within a region of interest and thus changes in density will be visible within the image, as in col. 4, lines 26-33. In one example, a spot within an image is comprised of 100 pixels, as in col. 4, lines 30-33. The spots are visualized within an image and this accommodates assessing the location and shape of the spots. Both variations in texture and the heterogeneity will be visible as variations in brightness from pixel to pixel within the scorable region or spot, which reflects variation in attenuation of the return data.

Applicants acknowledge these statements. However, while the Hu et al. images may inherently include information for determining size, shape and changes in density of spots data, Hu et al. does not determine and/or use the information in their assessing a patient's risk of cardiovascular disease. While clearly a risk assessment can be formulated based simply on a density profile of spots, Hu et al does not disclose, teach, suggest or even lead an ordinary artisan to include density, location, size, and shape data and change in density data in the calculation of the risk assessment. The change in density of spots is used in the present application to determine areas of abrupt changes in regional coronary elasticity. There is no disclose, teach, or suggest or even

anything to lead an ordinary artisan to determine areas of change in density let alone areas of abrupt changes in regional coronary elasticity.

Moreover, there is no teaching in Hu et al. that including these data would lead to an improved risk assessment. The secondary references add certain teachings to Hu et al., but the teaching are insufficient to render the present claims obvious. For these and other reasons set forth below, the currently claims are non-obvious over the main reference Hu et al and all secondary references in any and all combinations.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. **Claims 1 and 35-53** stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The Examiner states as follows:

> The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
>
> At least claims 1 and 43 (now claim 44) recite determining heterogeneity and texture of a calcified spot within an image, but the specification is not particular to these features. Claim 1 additionally recites determining a scatterness, but this also not disclosed. Claim 43(now claim 44) additionally recites performing each of two CT scans at different times and analyzing two or more sets of images generated at different times to determine changes in heterogeneity, texture and scatterness, but these features are not set forth in applicant's disclosure.
>
> Claim 47 defines the location metric as a distance from a base or apex of the heart, but this feature is not disclosed.
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> Claim 50 details analyzing texture for smoothness or roughness, but neither texture nor attributes of the lesions related to texture are disclosed as being analyzed.
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> Claim 51 discloses a density gradient comprising a higher density core or a higher density outer ring, but these features are not disclosed.
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> Claim 52 recites a step of identifying scattemess by interspot distances and determining the variance of densities among two or more spots, but these are not disclosed features of the invention.

Applicants have amended some of the claims and canceled others to address some of the 112, 1st paragraph rejections, expressly the following: "determining heterogeneity and texture of a calcified spot", "determining a scatterness", "changes in heterogeneity, texture and scatterness", "location metric as a distance from a base or apex of the heart", "analyzing texture for smoothness or roughness", "a density gradient comprising a higher density core or a higher density outer ring", "identifying scattemess by interspot distances and determining the variance of densities among two or more spots".

Applicants do not agree with the Examiner on the teaching of two or more scanning steps as the specification is clear that maps can be used to determine a progression of plaque and to categorize the patient's risk of cardiovascular disease using the maps: "using the map to determine progression of plaque; and b. using the determined plaque progression to categorize the patient's risk of cardiovascular disease." See original claims 15 and 29 an paragraphs [0004], [0027], [0029], and [0036]. To determine a progression requires multiple scans over time as a progression is defined as: "1: a sequence of numbers in which each term is related to its predecessor by a uniform law; 2 a :

the action or process of progressing : advance; b : a continuous and connected series : sequence." http://www.merriam-webster.com/dictionary/progression?show=0&t=1295020327. Thus, the specification is clearly sufficient to establish forming and using maps derived from CT scans to determine a progression of plaque and to categorize a patient's risk of cardiovascular disease based on these maps. A single map will not permit one to determine a progression. Only a sequence of scans can allow a progression to be determined.

Based on the cancellations, amendments and arguments, Applicants respectfully request withdrawal of these rejections.

Claim Rejections - 35 USC §103

2. **Claims 1, 38, 39, 40, 41, and 42** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (US 6,233,304) in view of Rather et al. (US 6,385,474).

The Examiner states as follows:

> Hu et al. disclose a method for detecting coronary artery calcification by computed tomography in one of multi-slice helical reconstruction and electron beam computed tomography in a system with multiple arrayed detectors (col. 1, lines 13-15; 42-62). Images are reconstructed based on the attenuation profile (col. 1, lines 19-21), with visualization of data giving rise to mapping sections of arteries or vessels of interest. The attenuation profile aids in identifying calcification (or scorable regions of interest or spots within the image) to determine calcification density, as in col. 1, lines 60-63 and col. 3, lines 48-53. A total calcium score is determined by summing the scores of the individual regions of interest, which indicates a risk as claimed. A density score is determined for each pixel within a region of interest (spot) and thus any changes in density will be observable, as in col. 4, lines 26-33. In one example, a spot or scorable region within an image is comprised of 100 pixels, as in col. 4, lines 30-33. The spots are visualized within an image and this accommodates assessing the location and shape of the spots. Plaques are understood to accumulate in both circular and angular formations. The pattern of the scorable regions (spots) will be visible within the image. Both variations in texture (rough or smooth) and heterogeneity will be visible as variations in brightness within the scorable region or spot, which reflects variation in attenuation of the return data. The method is disclosed to produce data for at least one or more regions of interest within the scorable region, as in col. 4, lines 56-60, abstract. In cases in which more than one region of interest is assessed, a variation in calcium density will be observable among the spots.
>
> The total calcium score determined in the method of Hu et al. is a general quantitative indicator for disease risk assessment. Calculation of x-ray attenuation coefficients is provided in the form of CT numbers that are used in threshold comparison (col. 4, lines 15-36, in which a threshold of 130 HU is selected).
>
> Hu et al. do not specifically address determining a scatterness for each calcified spot, but Rather et al. teach localizing features within a region of a CT image, for example, and collect scattering information in the form of reflection, trans!11ission and diffraction from features or spots within the object under examination, as in col. 2, line 44 - col. 3, line 3. The pattern of spots will be visible within the image.
>
> It would have been obvious to one ordinarily skilled in the art at the time of invention to incorporate assessment of scattering properties of a region of interest, as taught in Rather et al., in the method of Hu et al., in order to localize features or spots within the image.

Applicants have canceled claim 40 per 112, 1st paragraph rejection.

Hu et al do not disclose, teach or even lead an ordinary artisan to assign a risk score using anything but calcium density. Rather et al. discloses:

> In a preferred embodiment, the radiation sources and detectors cover a large solid angle, thereby substantially enclosing the object under study. As a result, a large fraction of all these types of secondary waves are detected by the radiation detectors. The resolution depends on the product of the number of sources and the number of detectors, which defines the number of resolution elements into which the volume occupied by the object under study may be divided.

Rather et al Col. 2, l. 62-Col. 3, l. 2.

The present claim 1 recites: analyzing the CT generated images to determine a location, shape, size, and density of each calcified spot in a patient's heart, analyzing the CT generated images to determine a distribution pattern of the calcified spots, defining a risk score based on the two analyzing steps, and assessing a patient's risk of cardiovascular disease based upon the risk score. The dependents claims add other limitations to claim 1, and Applicants direct their arguments to claim 1 in that if claim 1 is patentable over the combination of Hu et al and Rather et al, then dependent claims will be patentable as well.

The combination of Hu et al and Rather et al disclose and teach a risk assessment based solely on calcium density and localized intravascular lesions, but the combination does not disclose, teach or even direct an ordinary artisan to assess a risk score based on the location, shape, size, and density of each calcified spot (claim 1) in a patient's heart. Using these additional spot characteristics leads to an improved risk score for patients. Nothing in the combination of Hu et al and Rather et al would lead an ordinary artisan to utilize these additional characteristics in assessing a risk score for a patient.

Because the combination of Hu et al and Rather et al does not disclose, teach or even direct an ordinary artisan to assess a risk score based on the location, shape, size, and density of each calcified spot (claim 1) in a patient's heart, the combination cannot render claims 1, 38, 39, 41 and 21 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

3. **Claims 35 and 37** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (US 6,233,304) in view of Rather et al. (US 6,385,474), as applied to claim 1 above further in view of Tierstein et al. (US 200110018042).

The Examiner states as follows:

> The combination of Hu and Rather et al. includes all features of the invention as substantially claimed, as detailed above, and while changes in density will be visible with the thresholding to identify scorable regions (taken to be areas of greater risk of cardiovascular disease) in the method of Hu, it is not particularly disclosed that an change in density is identified as a high risk region; however, Tierstein et al. disclose CT visualization for detection of vulnerable plaques, in which likelihood or risk of a plaque destabilizing is assessed, as in [0007], [0071]. The methods are specific to identifying plaques most likely to rupture, or higher risk plaques, which are marked by a juncture in which pools of cholesterol abut areas of more fibrous plaques, as in [0015]. Identifying such a juncture is identifying an area of abrupt change. It is additionally disclosed that irregular plaque profiles are an indicator of thrombosis or a likelihood of complete occlusion, as in [0011], [0023]. It would have been obvious to one ordinarily skilled in the art at the time of invention to assess the CT images for areas of abrupt change in the arterial wall, as taught by Tierstein et al., in order to identify a potential for thrombosis or a complete occlusion, as in [0011].

Applicants reassert their contentions concerning Hu et al and Rather et al here. The Examiner adds Tierstein et al to try and plug the holes in the combination of Hu et al and Rather et al. Tierstein et al do indeed disclose analyzing aspects of vulnerable plaques, but Tierstein uses this information to assess a rick that a given plaque will rupture. However, Tierstein et al fail to disclose, teach or even suggest using information about calcified spots, such as shape, size, and density, to

produce a score to assess a patient's risk of cardiovascular disease.

Combining Hu et al, Rather et al and Tierstein et al yields a risk assessment based on density and on a risk that a particular plaque may rupture. However, such an analysis does not suggest the risk assessment of this invention. The risk assessments of this invention derive not only from the density of calcified spots, but also on their shape, size, and density. Nothing like the present scoring is even remotely suggested by the combination. Moreover, Hu et al and Rather et al does not suggest using an area of an abrupt change in regional coronary elasticity as a high-risk region, which effects the risk assessment, but is not a risk that that spot will rupture as in Tierstein et al.

Because the Hu et al, Rather et al and Tierstein et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, and density, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claims 35 and 37 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

4. **Claims 43 (now 44), 44 (now 45), 48, 49, 50, 51, 52, and 53** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. in view of Rather et al. and O'Brien et al. (US 2004/0057955).

The Examiner states as follows:

> Hu et al. disclose a method for detecting coronary artery calcification by computed tomography in one of multi-slice helical reconstruction and electron beam computed tomography in a system with multiple arrayed detectors (col. 1, lines 13-15; 42-62). Images are reconstructed based on the attenuation profile (col. 1, lines 19-21), with visualization of data giving rise to mapping sections of arteries or vessels of interest. The attenuation profile aids in identifying calcification (or scorable regions of interest or spots within the image) to determine calcification density, as in col. 1, lines 60-63 and col. 3, lines 48-53. A total calcium score is determined by summing the scores of the individual regions of interest, which indicates a risk as claimed. A density score is determined for each pixel within a region of interest (spot) and thus any changes in density will be observable, as in col. 4, lines 26-33. In one example, a spot or scorable region within an image is comprised of 100 pixels, as in col. 4, lines 30-33. The spots are visualized within an image and this accommodates assessing the location and shape of the spots. Plaques are understood to accumulate in both circular and angular formations. The pattern of the scorable regions (spots) will be visible within the image. Both variations in texture (rough or smooth) and heterogeneity will be visible as variations in brightness within the scorable region or spot, which reflects variation in attenuation of the return data. The method is disclosed to produce data for at least one or more regions of interest within the scorable region, as in col. 4, lines 56-60, abstract. In cases in which more than one region of interest is assessed, a variation in calcium density will be observable among the spots.
>
> The total calcium score determined in the method of Hu et al. is a general quantitative indicator for disease risk assessment. Calculation of x-ray attenuation coefficients is provided in the form of CT numbers that are used in threshold comparison (col. 4, lines 15-36, in which a threshold of 130 HU is selected).
>
> Hu et al. do not specifically address determining a scatterness for each calcified spot, but Rather et al. teach localizing features within a region of a CT image, for example, and collect scattering information in the form of reflection, transmission and diffraction from features or spots within the object under examination, as in col. 2, line 44 - col. 3, line 3. The pattern of spots will be visible within the image. It is understood that patterns associated with the density gradient, such as a higher density core or outer ring, will be apparent within the image and reflected in the attenuation data.
>
> It would have been obvious to one ordinarily skilled in the art at the time of invention to incorporate assessment of scattering properties of a region of interest, as taught in Rather et al, in the method of Hu et al., in order to localize features or spots within the image.
>
> The combination of Hu and Rather et al. includes all features of the invention as substantially claimed, but is not specific to scanning at first and second times; however, O'Brien et al. teach assessing aortic valve calcium for both an initial scan and a follow up scan, as in [0086]. A comparison

> is made such that any change in calcium accumulation over time can be assessed, as in [0089], which presumably involves storing or saving data resulting from a first scan for subsequent access. It would have been obvious to one ordinarily skilled in the art at the time of invention to collect data over two separate diagnostic scans at first and second times, such that the progression of plaque over the interval can be assessed, as taught in O'Brien et al. It is understood that the assessment of a calcified region or a lesion at a second time will offer an indication as to the outcome or resulting state of any lesion(s) localized in a first scan.

Applicants reassert their contentions concerning Hu et al and Rather et al here. O'Brien et al discloses arotic valve calcium scoring. This scoring is assessed progressively – multiple scans over time, but the scoring relates to calcification of the aortic valve and does not disclose risk scoring based on calcified spot shape, size, density and change in density.

Because the Hu et al, Rather et al and O'Brien et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, density and change in density, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claims 43 (now 44), 44 (now 45), 48, 49, 50, 51, and 52 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

The Examiner states as follows:

> Regarding claim 53, a progression of plaque is determined in O'Brien et al., as in [0089], in which accumulation over time is assessed between first and second scans. O'Brien et al. additionally teach statistically analyzing the data to assess progression of calcification, as in [0085].

Applicants reassert their contentions concerning Hu et al and Rather et al here. O'Brien et al discloses arotic valve calcium scoring. This scoring is assessed progressively – multiple scans over time, but the scoring relates to calcification of the aortic valve and does not disclose risk scoring based on calcified spot shape, size, density and change in density.

Because the Hu et al, Rather et al and O'Brien et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, density and change in density, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claim 53 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

5. **Claim 26 [36]** stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (US 6,233,304) in view of Rather et al. (US 6,385,474), as applied to claim 1 above, further in view of Zeng et al. (US 2003/0099385).

The Examiner states as follows:

> The combination of Hu and Rather et aI. includes all features of the invention as substantially claimed, including localizing atherosclerotic plaques within images, but is not specific to locating the lesions with respect to anatomical landmarks associated with the heart; however, Zeng et aI. teach segmenting lesions within CT images to determine their location(s) with respect to various landmarks, as in [0051]. It would have been obvious to one ordinarily skilled in the art at the time of invention to include referencing plaque distance from the heart or an anatomical feature of the heart, such that lesion locations can be determined with respect to identifiable structures also appearing in the image.

Applicants reassert their contentions concerning Hu et al and Rather et al here. Zeng et al

speak to locating lesions relative to landmarks, but fails to disclose, teach or even direct an ordinary artisan to determining proximal and distal artery calcification and using the data in risk assessment.

Because the Hu et al, Rather et al, and Zeng et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, density, change in density and proximal and distal artery calcification, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claim 36 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

6. **Claim 47** stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. in view of Rather et al. and O'Brien et al., as applied to claim 43 above, further in view of Zeng et al. (US 2003/0099385).

The Examiner states as follows:

> The combination ofHu, Rather and O'Brien et al. includes all features of the invention as substantially claimed, including localizing atherosclerotic plaques within images, but is not specific to locating the lesions with respect to anatomical landmarks associated with the heart; however, Zeng et al. teach segmenting lesions within CT images to determine their location(s) with respect to various landmarks, as in [0051]. It would have been obvious to one ordinarily skilled in the art at the time of invention to include referencing plaque distance from the heart or an anatomical feature of the heart, such that lesion locations can be determined with respect to identifiable structures also appearing in the image.

Applicants reassert their contentions concerning Hu et al, Rather et al and O'Brien et al here. Zeng et al speak to locating lesions relative to landmarks, but fails to disclose, teach or even direct an ordinary artisan to determining proximal and distal artery calcification and using the data in risk assessment.

Because the Hu et al, Rather et al, O'Brien et al and Zeng et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, density, change in density and proximal and distal artery calcification, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claim 53 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

7. **Claim 42 (now 43)** stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (US 6,233,304) in view of Rather et al. (US 6,385,474), as applied to claim 1 above, further in view of Kaufman et al. (US 2003/0018245).

The Examiner states as follows:

> The combination of Hu and Rather et al. includes all features of the invention as substantially claimed, including analyzing CT data associated with images of atherosclerotic plaques, but is not specific to statistical assessments; however, Kaufman et al. teach localization and analysis of lesions within CT images with methods applicable to calcium assessment and scoring, as in the abstract and [0050], and detail statistical analysis of the attenuation data, including identification of a range, mean and standard deviation, as in [0014], [0049], [0066]-[0067], [0123], [0133], [0136] and [0143]. It would have been obvious to one ordinarily skilled in the relevant art at the time of invention to include calculation of statistics for each lesion appearing in the image in order to gamer useful information about each nodule within an image.

Applicants reassert their contentions concerning Hu et al and Rather et al here. Kaufman et al simply adds the disclosure of standard mathematic attribute associated with a distribution. Kaufman et al add nothing to cure the basic deficiencies of the Hu et al and Rather et al combination.

Because the Hu et al, Rather et al, and Kaufman et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, density, and change in density, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claim 53 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

8. **Claim 46** stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. in view of Rather et al. and O'Brien et al., as applied to claim 43 above, further in view of Kaufman et al. (US 2003/0018245).

The Examiner states as follows:

> The combination of Hu, Rather and O'Brien et al. includes all features of the invention as substantially claimed, including analyzing CT data associated with images of atherosclerotic plaques, but is not specific to statistical assessments; however, Kaufman et al. teach localization and analysis of lesions within CT images with methods applicable to calcium assessment and scoring, as in the abstract and [0050], and detail statistical analysis of the attenuation data, including identification of a range, mean and standard deviation, as in [0014], [0049], [0066]- [0067], [0123], [0133], [0136] and [0143]. It would have been obvious to one ordinarily skilled in the relevant art at the time of invention to include calculation of statistics for each lesion appearing in the image in order to gamer useful information about each nodule within an image.

Applicants reassert their contentions concerning Hu et al, Rather et al and O'Brien et al here. Kaufman et al simply adds the disclosure of standard mathematic attribute associated with a distribution. Kaufman et al add nothing to cure the basic deficiencies of the Hu et al, Rather et al and and O'Brien et al combination.

Because the Hu et al, Rather et al, O'Brien et al and Kaufman et al combination does not disclose, teach or even lead an ordinary artisan to construct a risk score using calcified spot shape, size, density, and change in density, to produce a score to assess a patient's risk of cardiovascular disease, the combination cannot render claim 53 obvious. Applicants, therefore, respectfully request withdrawal of this rejection.

If it would be of assistance in resolving any issues in this application, the Examiner is kindly invited to contact applicant's attorney Robert W. Strozier at 713.977.7000

The Commissioner is authorized to charge or credit Deposit Account 501518 for any additional fees or overpayments.

Respectfully submitted,

Date: **19 January 2011**

/Robert W. Strozier/

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